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Letter to the Editor

Company Reply to "Unexpected Outbreak of Epstein-Barr Virus Post-Transplantation Lymphoproliferative Disorder after Hematopoietic Stem Cell Transplantation Conditioning with Thymoglobulin"

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To the Editor,

In a "Letter to the Editor" by Yanez et al. [1], 8 cases of post-transplantation lymphoproliferative disorder (PTLD) were reported, 5 occurring between December 2011 and June 2012. This prompted the authors' center to stop using Thymoglobulin (Genzyme Polyclonals, Lyon, France) for graft-versus-host disease prophylaxis in allogeneic hematopoietic stem cell transplantation.

The authors speculate that the higher incidence of PTLD seen at their center was due to a change in the manufacturing process of Thymoglobulin, leading to a change in the product's potency. In particular, the authors' state that in 2007 a change in the quantity of the thymic source for rabbit immunization for Thymoglobulin production was undertaken without clinical validation. Sanofi would like to address the authors' claims concerning the safety aspects, manufacturing process, and potency testing of Thymoglobulin and the regulatory steps required for approval of such changes.

Thymoglobulin safety is evaluated on a regular basis, and periodic updates are submitted to health authorities by the company's pharmacovigilance department. Unsolicited reporting rates of PTLD from 2008 to 2014 were comparable with earlier reporting rates observed from 2004 to 2007. In reported cases of PTLD, Thymoglobulin was often used in combination with other immunosuppressive agents. The type and intensity of the immunosuppressive therapy may vary across patients and institutions and might impact the risk of developing PTLD.

The interpretation of the authors on the impact of the changes in the Thymoglobulin manufacturing process is not substantiated. The reduction of the number of thymic cells used to immunize rabbits used to make Thymoglobulin does not impact on the quality of the final product. All parameters indicative of a potential change in the nature of both serums and final products have been evaluated, and following a strictly regulated procedure, the manufacturing process updates were submitted to and approved by the Health Authorities of all 68 countries where Thymoglobulin is registered. Tests of the biological activity for horse and rabbit antithymocyte globulins are described in the Monograph of Antithymocyte Globulins [2]. The standard method to evaluate biological activity of antithymocyte globulins, according to the current European monograph, is complement dependent cell lysis. This required release test is stable, well controlled, validated, and approved by Health Authorities worldwide. Released lots are tested on a regular basis during the shelf-life of thymoglobulin.

Sanofi is committed to producing high-quality products that meet or exceed established regulatory requirements in place to ensure safe and efficacious patient care.

REFERENCES

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2. Monograph of antithymocyte globulins. In European pharmacopoeia, version 8.0., 2013. Strasbourg, Council of Europe.

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